

WHAT IS CLAIMED IS:

1 1. A method of screening a candidate species for its ability to evoke a
2 response in a target that produces a change in the environment of said target species, said
3 method comprising:

- 4 (a) forming a capsule containing said candidate species with said target and
5 an intelligent substance which is defined as a substance that undergoes a
6 transformation upon exposure to said change in environment, said candidate species
7 and said target isolated from each other in said capsule and yet capable of being
8 placed in contact by an externally imposed condition;
- 9 (b) imposing said condition on said capsule, thereby placing said candidate
10 species and said target in contact; and
- 11 (c) monitoring said capsule for an indication of said transformation in said
12 intelligent substance.

1 2. A method in accordance with claim 1 in which said target is a
2 biological cell.

1 3. A method in accordance with claim 1 in which said target is an
2 enzyme.

1 4. A method in accordance with claim 1 in which said target is a
2 biological receptor.

1 5. A method in accordance with claim 4 in which said biological receptor
2 is an intracellular receptor selected from the group consisting of estrogen receptors,
3 glucocorticoid receptors, androgen receptors, progesterone receptors, and mineralocorticoid
4 receptors.

1 6. A method in accordance with claim 1 in which said target is a
2 transcription factor.

1 7. A method in accordance with claim 1 in which said target is a kinase.

1 8. A method in accordance with claim 1 in which said target is a member
2 selected from the group consisting of proteins, sugars, nucleic acids, and lipids.

1 **9.** A method in accordance with claim **1** in which said target is an enzyme
2 and said response is inhibition of said enzyme.

1 **10.** A method in accordance with claim **1** in which said target is a
2 biological receptor and said response is activation of said receptor.

1 **11.** A method in accordance with claim **1** in which said target is a
2 biological receptor and said response is an inhibition of the activation of said receptor due to
3 competition for said receptor between said candidate species and a natural activator of said
4 receptor.

1 **12.** A method in accordance with claim **1** in which said target is a
2 biological cell and said response is agonist action on a receptor of said biological cell and a
3 consequent intracellular process mediated by said agonist action.

1 **13.** A method in accordance with claim **1** in which said target is a
2 biological cell and said response is antagonist action on a receptor of said biological cell and
3 a consequent diminishment of an intracellular process due to said antagonist action.

1 **14.** A method in accordance with claim **1** in which said candidate species
2 is a single molecular species.

1 **15.** A method in accordance with claim **1** in which said candidate species
2 is a combination of molecular species.

1 **16.** A method in accordance with claim **1** in which said indication of said
2 transformation in said intelligent substance is a member selected from the group consisting of
3 a change in size of said capsule, a change in shape of said capsule, a change in an optical
4 property of said intelligent substance, a release of a detectable species from said capsule, and
5 an emission of a detectable signal from said capsule.

1 **17.** A method in accordance with claim **16** in which said indication of said
2 transformation in said intelligent substance is a change in size of said capsule.

1 **18.** A method in accordance with claim **16** in which said indication of said
2 transformation in said intelligent substance is a change in shape of said capsule.

1 **19.** A method in accordance with claim **1** in which said intelligent
2 substance is a crosslinked polymer and said change in environment is the release of an agent
3 that disrupts the crosslinking in said polymer, thereby causing said polymer to swell.

1 **20.** A method in accordance with claim **19** in which said polymer is
2 crosslinked by antigen-antibody interaction between polymer chains to which antigen and
3 antibody are covalently bound, and said change in environment is the release of free antigen
4 or antibody that competes with said antigen-antibody interaction between polymer chains.

1 **21.** A method in accordance with claim **19** in which said polymer is
2 crosslinked by a linking group that is cleavable by an enzyme, and said change in
3 environment is the release of said enzyme.

0 1 **22.** A method in accordance with claim **21** in which said linking group is a
2 β-galactoside, and said change in environment is the release of β-galactosidase.

1 **23.** A method in accordance with claim **16** in which said indication of said
2 transformation in said intelligent substance is a change in fluorescence of said capsule.

1 **24.** A method in accordance with claim **23** in which said change in
2 fluorescence of said capsule is a fluorescence emission from an otherwise non-fluorescing
3 capsule or an increase in fluorescence emission from said capsule.

1 **25.** A method in accordance with claim **24** in which said intelligent
2 substance comprises a support matrix with a fluorophore bound thereto, and said change in
3 environment is the release of a cleaving agent that cleaves said fluorophore said support
4 matrix, thereby causing a fluorescence emission.

1 **26.** A method in accordance with claim **25** in which said fluorophore is a
2 5-alkanoylaminofluorescein di-β-galactopyranoside, and said cleaving agent is β-
3 galactosidase.

1 **27.** A method in accordance with claim **24** in which said intelligent
2 substance comprises a crosslinked polymer with a fluorescence resonance energy transfer
3 pair bound thereto and spaced apart to produce no net fluorescence, and said change in

4 environment is the release of an agent that disrupts the crosslinking in said polymer, thereby
5 changing the spacing of said energy transfer pair and producing a net fluorescence.

1 **28.** A method in accordance with claim **1** in which said candidate species
2 is a chemical compound.

1 **29.** A method in accordance with claim **28** in which said candidate
2 compound is releasably immobilized on a solid support and said target is shielded from said
3 solid support by a barrier that is impermeable to said solid support yet permeable to said
4 candidate compound, and said externally imposed condition is a condition that causes release
5 of said candidate compound from said solid support.

1 **30.** A method in accordance with claim **29** in which said solid support is a
2 bead whose longest linear dimension is from about 1 nm to about 1 mm.

1 **31.** A method in accordance with claim **29** in which said solid support is a
2 bead whose longest linear dimension is from about 0.5 µm to about 500 µm.

1 **32.** A method in accordance with claim **29** in which said candidate
2 compound is covalently bonded to said solid support, and said externally imposed condition
3 is a condition that causes cleavage of said candidate compound from said solid support.

1 **33.** A method in accordance with claim **32** in which said candidate
2 compound is covalently bonded to said solid support through a nucleic acid linking group
3 with a restriction site and step (b) comprises impregnating said capsule with a restriction
4 enzyme effective to cause cleavage at said restriction site.

1 **34.** A method in accordance with claim **32** in which said candidate
2 compound is covalently bonded to said solid support through a photocleavable linking group
3 and step (b) comprises irradiating said capsule with light at a wavelength effective to cause
4 cleavage of said linking group.

1 **35.** A method in accordance with claim **34** in which said photocleavable
2 linking group is cleavable by ultraviolet light, said barrier shielding said biological cell from
3 said solid support is a casing that is impermeable to ultraviolet light, and step (b) comprises
4 irradiating said capsule with ultraviolet light.

1 **36.** A method in accordance with claim **1** in which step (a) comprises
2 encasing said candidate species in a shell and forming said capsule around said shell with
3 said target species external to said shell, and said externally imposed condition is a condition
4 that renders said shell permeable to said candidate species.

1 **37.** A method in accordance with claim **36** in which said shell is absorptive
2 of electromagnetic radiation and rupturable by heat and step (b) comprises irradiating said
3 shell with electromagnetic radiation.

1 **38.** A method in accordance with claim **36** in which said shell encasing
2 said candidate species is impermeable to said candidate species and is defined as a first shell
3 and said target is surrounded by a second shell which is permeable to said candidate species
4 and outside said first shell, said first shell being light absorptive and rupturable by heat and
5 said second shell being transparent, and step (b) comprises irradiating said capsule with light
6 thereby causing said first shell to rupture due to heat caused by light absorption without
7 rupture of said second shell.

1 **39.** A method in accordance with claim **36** in which said shell encasing
2 said candidate species is impermeable to said candidate species and said target is embedded
3 in a matrix that is outside said shell and permeable to said candidate species, and step (b)
4 comprises rupturing said shell.

1 **40.** A method in accordance with claim **36** further comprising encasing a
2 plurality of magnetic particles in said shell with said candidate species, and step (b)
3 comprises imposing a magnetic field on said capsule causing said magnetic particles to align
4 and thereby rupture said shell.

1 **41.** A method in accordance with claim **36** further comprising encasing a
2 plurality of magnetic particles in said shell with said candidate species, and step (b)
3 comprises imposing a magnetic field on said capsule to impart oscillating movement to said
4 magnetic particles, said movement causing rupture of said shell.

1 **42.** A method in accordance with claim **36** in which said shell comprises a
2 material that is contractible upon exposure to an external stimulus, and step (b) comprises

3 exposing said shell to said external stimulus to cause contraction of said material sufficient to
4 form channels through said shell for escape of said candidate species.

1 **43.** A method in accordance with claim **36** further comprising encasing
2 within said shell a solid particle which either contracts or expands upon exposing said shell to
3 an external stimulus, and step (b) comprises exposing said shell to said external stimulus to
4 cause sufficient contraction or expansion to rupture said shell.

1 **44.** A method in accordance with claim **1** in which step (a) comprises
2 sequestering said candidate species in a swollen hydrogel and forming said capsule around
3 said hydrogel with said target external to said hydrogel, and said externally imposed
4 condition is a condition that causes said hydrogel to contract and thereby expel said candidate
5 species for contact with said target.

1 **45.** A method of screening a plurality of candidate species for their ability
2 to evoke a response in a target that produces a change in the environment of said target
3 species, said method comprising:

4 (a) forming a plurality of capsules, each capsule containing one of said
5 candidate species, a plurality of said target species, and an intelligent substance which
6 is defined as a substance that undergoes a transformation upon exposure to said
7 change in environment, said candidate species in each capsule isolated from said
8 target in the same capsule and yet capable of being placed in contact with said target
9 by an externally imposed condition;

10 (b) imposing said condition on said plurality of capsules, thereby placing said
11 candidate species in contact with said target; and

12 (c) monitoring said capsules for an indication of said transformation in said
13 polymer and identifying the candidate species contained in a capsule that exhibits said
14 indication.

1 **46.** A method in accordance with claim **45** in which each candidate species
2 is a single molecular species.

1 **47.** A method in accordance with claim **45** in which each candidate species
2 is a combination of at least two distinct molecular species.

1 **48.** A method in accordance with claim **45** in which said candidate species
2 are chemical compounds that are releasably immobilized on microbeads with each candidate
3 compound on a separate microbead and at most one microbead retained in each capsule, and
4 said externally imposed condition is a condition that causes release of candidate compounds
5 from all of said microbeads.

1 **49.** A method in accordance with claim **45** in which said candidate species
2 are chemical compounds that are releasably immobilized on microbeads on which are also
3 immobilized identifier tags, each microbead having immobilized thereon a single candidate
4 compound and a single identifier tag which comprises a detectable code that is decipherable
5 to indicate the molecular structure of the candidate compound, and said externally imposed
6 condition is a condition that causes release of all of said candidate compounds from said
7 microbeads.

1 **50.** A method in accordance with claim **45** in which said candidate species
2 are peptides.

1 **51.** A method in accordance with claim **49** in which said candidate species
2 are peptides and each identifier tag is an oligonucleotide comprised of a sequence of codons
3 corresponding to the sequence of amino acids in the peptide immobilized on the same
4 microbead as said tag.

1 **52.** A method in accordance with claim **49** in which said candidate species
2 are chemical compounds and are immobilized on said microbeads in a manner that permits
3 release of said chemical compounds without releasing said identifier tags.